REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 23-43 presently appear in this application, with claims 37-43 withdrawn by the examiner as being directed to non-elected inventions, and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

The amendment to claim 23 to recite for "1 to 3 times" is supported in the present specification in the bottom half of page 11, and the amendment to claims 23 and 39-41 to recite for "100 μg or more" is supported at page 3, lines 6-7 from the bottom and page 7, third full paragraph.

The amendment to claims 25, 28 and 29 to recite "incorporated into the animal cell either simultaneously or successively" is supported in the present specification in the sentence bridging pages 11 and 12.

Claims 23-36 have been rejected under 35 U.S.C. 112, first paragraph, because the examiner states that the specification, while being enabling for a process for producing a recombinant fibrinogen producing cell which produces a high level of fibrinogen by incorporating into an animal cell, genes encoding an α chain, a β chain, and a γ chain, does not reasonably provide enablement for a process for producing a recombinant fibrinogen producing cell which produces a high level

of fibrinogen by incorporating into an animal cell a gene encoding a variant of an α chain, a variant of a β chain, and a variant of a γ chain.

This rejection is obviated by the amendment to claim 23, without prejudice, to recite for the αE and γ′ variants, as supported in the present specification at page 9, lines 4-5, and page 2, first paragraph, instead of for any variant thereof.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 23-36 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The examiner holds that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

This rejection is also obviated by the amendment to claim 23, without prejudice, to recite for the αE and γ′ variants instead of for any variant thereof.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 23-36 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly

point out and distinctly claim the subject matter which applicant regards as the invention.

This rejection is obviated by the amendments to the claims to correct grammatical and idiomatic errors as well the amendments to claims 23-29 to clear up the specific indefiniteness issues raised by the examiner in this rejection.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 23-24, 29, and 32-34 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Roy et al., *Journal of Biological Chemistry* 266(8):4758-4763 (1991). For examination purposes, the examiner states that claim 23 has been interpreted as a process for producing a recombinant fibrinogen producing cell which produces recombinant fibrinogen, wherein said process comprises incorporating into an animal cell, genes encoding an α chain, a β chain, and a γ chain. This rejection is respectfully traversed.

The only disclosure in the cited and applied Roy reference of preparing cells that can produce all three of the α, β, and γ chains of fibrinogen is when <u>equal amounts</u> of all three expression vectors, each expressing a different chain, were used to transfect COS-1 cells to obtain a stable cell line (see page 4759, right column, second paragraph of the section entitled "Transfection and Selection of Stable Cell Lines"). There is no

teaching whatsoever in Roy that would lead one of ordinary skill in the art to use unequal amounts of the genes encoding the three chains, much less specifically the unequal amounts in a ratio of (α+β):γ of 1:1 to 1:3, as positively recited in the present claims. See also the present specification near the bottom of page 11, where the specific ratios of the genes for the individual chains, i.e., α:β:γ of 1:1:2 to 1:1:6 (which is the same as a ratio of (α+β):γ of 1:1 to 1:3). Thus, Roy's disclosures and teachings simply cannot lead one of ordinary skill in the art to arrive at the presently claimed invention where a high level of fibrinogen (100 µg/ml or more) is capable of being produced in the recombinant fibrinogen-producing cell. Note that in the "Quantitation of Secreted Fibrinogen" section in the left column on page 4760 of Roy, the concentration range of the standard curve using pure human fibrinogen is from 0.25-4.0 µg/ml and it stands to reason that this is the concentration range measured for fibrinogen secreted into the culture media from the COS-α,β,γ cells. This appears to be confirmed by the disclosure in the last sentence of the Results in the left column on page 4762 of Roy that an average of 2.08 µg of fibrinogen was secreted in 24 hrs. The production level of at least 100 µg/ml that the cells prepared by the presently claimed method are capable of producing is far above the production level taught in Roy. It would certainly not have been obvious and predictable to

one of ordinary skill in the art that unequal numbers of genes for the α, β and γ chains, as specified in the presently amended claims, would cause the cells to produce such a high level of fibrinogen.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 25, 26 and 28 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Roy et al. in view of Lord et al., *Blood Coagulation and Fibrinolysis* 4(1):55 (1993), abstract only. The examiner states that Roy does not teach an expression vector encoding more than one fibrinogen chain but asserts that Lord teaches that fibrinogen chains can be individually cloned into the same expression vector. This rejection is respectfully traversed.

The rejected claims all ultimately depend from independent claim 23. The teachings of Lord as a secondary reference does not fulfill the deficiencies of the primary Roy reference as discussed above insofar as independent claim 23 (and claims dependent therefrom) are concerned. The combination of Roy and Lord would still not lead one of ordinary skill in the art to use the specified ratio of the genes of the fibrinogen chains, as recited in the present claims, to arrive at the presently claimed method which prepares cell to produce a high level of fibrinogen of 100 μg or more.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 35-36 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Roy et al. in view of Lord (US 6037457). The examiner states that while Roy does not teach CHO cells, the secondary Lord reference teaches that recombinant fibrinogen can be expressed using CHO cells. This rejection is respectfully traversed.

Just as discussed above in the immediately preceding rejection, the secondary Lord cited and applied in this rejection also does not fulfill the deficiencies of the primary Roy reference. For the same reasons that independent claim 23 is not obvious, dependent claims 35 and 36 are also not obvious. Thus, the combination of Roy and Lord would still not lead one of ordinary skill in the art to use the specified ratio of the genes of the fibrinogen chains, as recited in the present claims, to arrive at the presently claimed method which prepares cell to produce a high level of fibrinogen of 100 μg or more.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 30-31 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Roy et al. in view of Lord (US 6037457) in view of Estes et al. (US 7423135). The examiner states that Roy in view of Lord do not teach chicken β-actin

promoter and a dhfr gene. However, the examiner contends that Estes makes up for this lack of teaching in Roy and Lord by disclosing that chicken β-actin promoter can be employed with a dhfr gene in a suitable expression system for CHO cells. This rejection is respectfully traversed.

Rejected claims 30 and 31 are also ultimately dependent from claim 23. The teaching in Estes of using chicken β-actin promoter with a dhfr gene in a suitable expression system for CHO cells does not fulfill the deficiencies in Roy (and Lord) as discussed above. Accordingly, the combination of Roy, Lord and Estes simply cannot lead one of ordinary skill in the art to the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 37-43 withdrawn by the examiner have been amended to be consistent with the amendments to the elected claims. Furthermore, withdrawn claim 37 is now made dependent from claim 23, reciting that the method of claim 23 <u>further comprises</u> incorporating a baculovirus P35 gene. Claim 37, as amended should be rejoined with the elected claims since the search conducted on the elected method would have certainly encompassed/covered the additional feature recited in claim 37 as well. Accordingly, there is no serious burden as required for a restriction requirement to be proper.

In addition, it is believed that the present claims all share a special technical feature that indeed defines a special contribution over the cited and applied Roy reference and the prior art. Accordingly, rejoinder of the withdrawn claims, and particularly withdrawn method claim 37, is respectfully requested.

In view of the above, the claims comply with 35 USC 112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By /ACY/
Allen C. Yun
Registration No. 37,971

ACY:jhw
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
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